This Page Is Inserted by IFW Operations and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents will not correct images, please do not report the images to the Image Problem Mailbox.

Amendments to the Claims:

The following listing of claims replaces all prior versions and listings of claims in this application.

- 1. (currently amended) A backbone cyclized peptide analog having IL-6 antagonist activity, comprising a peptide sequence of five to twenty amino acids that incorporates at least one building unit, said building unit containing one nitrogen atom of the peptide backbone connected to a bridging group eomprising having the structure

 -(CH₂)_m Y² (CH₂)_n , wherein m and n are 1 to 5, and wherein Y² is an amide, thioether, thioester or disulfide, wherein the at least one building unit is connected via the bridging group to form a cyclic structure.
- 2. (original) The backbone cyclized analog of claim 1 wherein the peptide sequence comprises six to twelve amino acids.
- 3. (original) The backbone cyclized analog of claim 1 wherein the peptide sequence incorporates at least one D-isomer of an amino acid.
- 4. (original) The backbone cyclized analog of claim 1 wherein the peptide sequence incorporates at least two D-isomers of an amino acid.
- 5. (original) The backbone cyclized analog of claim 1 wherein the linear peptide sequence is derived from the IL-6 receptor.
- 6. (original) The backbone cyclized analog of claim 1 wherein the linear peptide sequence is derived from the IL-6 molecule.
- 7. (currently withdrawn) The backbone cyclized analog of claim 1 having the general formula 1:

Formula No. 1

```
wherein m and n are 1 to 5;
```

X designates a terminal carboxy acid, amide or alcohol group;

R²⁴⁹ is Trp, (L) or (D)Lys, (L) or (D) Tyr or (D)Phe;

R²⁵⁰ is Arg;

R²⁵¹ is (L) or (D)Leu or Lys;

R²⁵² is (L) or (D)Arg;

R²⁵³ is (D)- or (L)- Phe;

R²⁵⁴ is Ala;

R²⁵⁵ is (D)- or (L)- Leu or is Lys;

R²⁵⁶ is absent or is (L) or (D) Arg;

R²⁵⁷ is (L) or (D) Tyr;

R²⁵⁸ is Ala; and

Y² is amide, thioether, thioester or disulfide.

8. (currently withdrawn) The backbone cyclized analog of claim 7 wherein

 R^{249} is Trp, (L)- or (D)- Lys or (D)Phe;

R²⁵⁰ is Arg;

R²⁵¹ is Lys or (D)Leu;

R²⁵² is (D)Arg;

R²⁵³ is (D)- or (L)- Phe;

R²⁵⁴ is Ala;

R²⁵⁵ is (D)- or (L)- Leu;

R²⁵⁶ is absent or is Arg;

R²⁵⁷ is (D)Tyr;

 R^{258} is Ala; and

Y² is amide, thioether, thioester or disulfide.

9. (currently withdrawn) The backbone cyclized IL-6 antagonist of claim 8 having the formula:

Trp-Arg-Lys-(D)Arg-Phe-AlaC3-Leu-Arg-(D)Tyr-AlaN3-NH2

10. (currently withdrawn) The backbone cyclized IL-6 antagonist of claim 8 having the formula:

(D)Lys-Arg-(D)Leu-(D)Arg-(D)Phe-AlaC3-(D)Leu-Arg-(D)Tyr-AlaN3-NH2

11. (currently withdrawn) The backbone cyclized IL-6 antagonist of claim 8 having the formula:

Claims 12 to 28. (cancelled)

29. (previously presented) The backbone cyclized analog of claim 1 having the general formula:

$$R^{1}-NR^{2}-R^{3}-R^{4}-R^{5}-NR^{6}-R^{7}-X$$

$$\left[(CH_{2})_{m}-Y^{2}-(CH_{2})_{n} \right]$$

wherein m and n are 1 to 5;

X designates a terminal carboxy acid, amide or alcohol group;

R¹ is (D)Bip, Gln, Lys, Lys(ZCL) Dab or absent;

R² is (L) or (D)Lys, Gly, Ala, (D)Phe or Trp;

R³ is (D) Cit, Lys, (D)Bip or absent;

R⁴ is Orn, 4PyrAla, (L) or (D)Dab, (L) or (D)Arg, Lys or Dpr;

R⁵ is HomArg, Orn, Lys, Lys(ZCL), Arg, Arg(Mtr) or (D)Glu;

R⁶ is Asn, (L) or (D)Trp, (D)Gln or (D)Ala;

R⁷ is Arg, (L) or (D)Trp, (L) or (D)Gln, Abu, Glu or (p-NO₂)Phe; and

Y² is amide, thioether, thioester or disulfide.

30. (currently amended) The backbone cyclized analog of claim 29 A backbone cyclized peptide analog having IL-6 antagonist activity, having the general formula 3:

$$R^1$$
---N R^2 --- R^3 ---- R^4 ----N R^5 --- R^6 -X
$$\begin{bmatrix} CH_2 & -Y^2 - (CH_2) & -Y^2 \end{bmatrix}$$
Formula No. 3

wherein m and n are 1 to 5;

X designates a terminal carboxy acid, amide or alcohol group;

R1 is (D)Bip, Gln, Lys, Lys(ZCL) or Dab;

R² is (D)Lys, Gly, Ala or Trp

R³ is Orn, 4PyrAla, (L) or (D)Dab, (D)Arg, Lys or Dpr;

R⁴ is Lys, Lys(ZCL), Arg, Arg(Mtr) or (D)Glu;

R⁵ is Asn, Trp or (D)Ala;

R⁶ is Arg, (p-NO₂)Phe, (L) or (D)Trp, Gln, Abu or Glu; and

Y² is amide, thioether, thioester or disulfide.

31. (withdrawn) The backbone cyclized analog of claim 29 having the general formula 4:

Formula No. 4

wherein m and n are 1 to 5;

X designates a terminal carboxy acid, amide or alcohol group;

R¹ is (D)Phe or Lys;

R² is (D)Cit, Lys or (D)Bip;

R³ is Dpr, 4PyrAla or (L) or (D)Arg;

R⁴ is HomArg, Orn or Lys;

R⁵ is (D)Gln or (L) or (D) Trp;

 R^6 is (L) or (D)Gln or (p-NO₂)Phe; and

Y² is amide, thioether, thioester or disulfide.

32. (Currently Amended) A pharmaceutical composition comprising a backbone cyclized IL-6 antagonist comprising a peptide sequence of five to twenty amino acids that

incorporates at least one building unit, said building unit containing one nitrogen atom of the peptide backbone connected to a bridging group eomprising having the structure $-(CH_2)_m - Y^2 - (CH_2)_n -$, wherein m and n are 1 to 5, and wherein Y^2 is an amide, thioether, thioester or disulfide, wherein the at least one building unit is connected via the bridging group to form a cyclic structure, together with a pharmaceutically acceptable carrier or diluent.

33. (Previously presented) The pharmaceutical composition of claim 32 14 wherein the IL-6 antagonist is a backbone cyclized peptide analog having the general formula 1:

Formula No. 1

wherein m and n are 1 to 5;

X designates a terminal carboxy acid, amide or alcohol group;

R²⁴⁹ is Trp, (L) or (D)Lys, (L) or (D)Tyr or (D)Phe;

R²⁵⁰ is Arg;

R²⁵¹ is (L) or (D)Leu or Lys;

R²⁵² is (L) or (D)Arg;

R²⁵³ is (D) or (L)Phe;

R²⁵⁴ is Ala;

R²⁵⁵ is (D) or (L)Leu or is Lys;

R²⁵⁶ is absent or is (L) or (D)Arg;

 R^{257} is (L) or (D)Tyr;

R²⁵⁸ is Ala; and

Y² is amide, thioether, thioester or disulfide.

34. (withdrawn) The pharmaceutical composition of claim 33 wherein the IL-6 antagonist is a backbone cyclized peptide analog having the formula:

- 35. (withdrawn) The pharmaceutical composition of claim 33 wherein the IL-6 antagonist is a backbone cyclized peptide analog having the formula:
 - (D)Lys-Arg-(D)Leu-(D)Arg-(D)Phe-AlaC3-(D)Leu-Arg-(D)Tyr-AlaN3-NH₂
- 36. (withdrawn) The pharmaceutical composition of claim 33 wherein the IL-6 antagonist is a backbone cyclized peptide analog having the formula:
 - (D)Phe-Arg-(D)Leu-(D)Arg-(D)Phe-AlaC3-Leu-(D)Tyr-AlaN3-NH₂
- 37. (previously presented) The pharmaceutical composition of claim 32 wherein the IL-6 antagonist is a backbone cyclized peptide analog having the general formula:

$$R^{1}-NR^{2}-R^{3}-R^{4}-R^{5}-NR^{6}-R^{7}-X$$

$$CH_{2}_{m}-Y^{2}-CCH_{2}_{n}$$

wherein m and n are 1 to 5;

X designates a terminal carboxy acid, amide or alcohol group;

R1 is (D)Bip, Gln, Lys, Lys(ZCL) Dab or absent;

R2 is (L) or (D)Lys, Gly, Ala, (D)Phe or Trp;

R3 is (D) Cit, Lys, (D)Bip or absent;

R4 is Orn, 4PyrAla, (L) or (D)Dab, (L) or (D)Arg, Lys or Dpr;

R5 is HomArg, Orn, Lys, Lys(ZCL), Arg, Arg(Mtr) or (D)Glu;

R6 is Asn, (L) or (D)Trp, (D)Gln or (D)Ala;

R7 is Arg, (L) or (D)Trp, (L) or (D)Gln, Abu, Glu or (p-NO2)Phe; and

Y² is amide, thioether, thioester or disulfide.

38. (Currently amended) The A pharmaceutical composition of claim 37 comprising a backbone cyclized IL-6 antagonist wherein the IL-6 antagonist is a backbone cyclized peptide analog having has the general formula 3:

$$R^{1}$$
 --- R^{2} --- R^{3} --- R^{4} --- R^{5} --- R^{6} - R^{6

Formula No. 3

wherein m and n are 1 to 5;

X designates a terminal carboxy acid, amide or alcohol group;

R1 is (D)Bip, Gln, Lys, Lys(ZCL) or Dab;

R² is (D)Lys, Gly, Ala or Trp

R³ is Orn, 4PyrAla, (L) or (D)Dab, (D)Arg, Lys or Dpr;

R⁴ is Lys, Lys(ZCL), Arg, Arg(Mtr) or (D)Glu;

R⁵ is Asn, Trp or (D)Ala;

R⁶ is Arg, (p-NO2)Phe, (L) or (D)Trp, Gln, Abu or Glu; and

Y² is amide, thioether, thioester or disulfide.

39. (withdrawn) The pharmaceutical composition of claim 37 wherein the IL-6 antagonist is a backbone cyclized peptide analog having the general formula 4:

$$\begin{bmatrix} NR^{1} - R^{2} - R^{3} - R^{4} - NR^{5} - R^{6} - X \\ CH_{2} & - CH_{2} \end{bmatrix}$$

Formula No. 4

wherein m and n are 1 to 5;

X designates a terminal carboxy acid, amide or alcohol group;

R¹ is (D)Phe or Lys;

R² is (D)Cit, Lys or (D)Bip;

R³ is Dpr, 4PyrAla or (L) or(D)Arg;

R⁴ is HomArg, Orn or Lys;

R⁵ is (D)Gln or (L) or (D)Trp;

R⁶ is (L) or (D)Gln or (p-NO₂)Phe; and

Y² is amide, thioether, thioester or disulfide.